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EXAMINER	
POLANSKY, GREGG	
ART UNIT	**PAPER NUMBER**
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/651,305	WANG, CHIA-GEE	
	Examiner	Art Unit	
	Gregg Polansky	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 October 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-99* is/are pending in the application.

4a) Of the above claim(s) *See Continuation Sheet* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,5,7,12,13,16-36,38,40,42,47,48,51-65,67,69,71,76-88,90,92 and 97-99* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *28 August 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/27/2003*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims withdrawn from consideration are 2,4,6,8-11,14,15,37,39,41,43-46,49,50,66,68,70,72-75,89,91 and 93-96.

DETAILED ACTION

Status of Claims

1. Applicant's amendments of Claims 36, 65, and 85-99, filed 10/23/2006, are acknowledged.

2. Applicant's Information Disclosure Statement, filed 10/27/2003, is acknowledged.

3. Applicant's election of the species/compound cisplatin, without traverse, in the reply filed on 9/12/2007 is acknowledged. The Election of Species Requirement is thus deemed to be proper and is made Final.

4. Claims 1-99 are pending.

5. Claims 2, 4, 6, 8-11, 14, 15, 37, 39, 41, 43-46, 49, 50, 66, 68, 70, 72-75, 89, 91 and 93-96 are withdrawn from consideration because they do not read on the elected species (cisplatin). 37 CFR 1.142(b).

6. Claims 1, 3, 5, 7, 12, 13, 16-36, 38, 40, 42, 47, 48, 51-65, 67, 69, 71, 76-88, 90, 92 and 97-99 are under consideration.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 17, 19, 20, 22-24, 52, 54-59, 78, 80-88, 90, 92, and 97-99 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "substantially" in Claims 17, 20, 22, 52, 55, 57, 78, 80, and 82 is a relative term, which renders the claims indefinite. The term is not defined by the claims, the Specification does not provide a reasonable standard for ascertaining the requisite degree, and thus one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Since no guidance is provided as to how "substantial" a given value is and still falls within the scope of the instantly claimed subject, the metes and bounds of the term are not clear, making it impossible to ascertain with reasonable precision when that term is infringed and when it is not.

The term "up to about" in Claims 19, 54, 79, and 87 renders the claims indefinite because it does not adequately define the metes and bounds of the claims (i.e., it does not set a lower limit for the thickness of the target of the e-beam generated by the x-ray tube).

The terms "above and near" in Claims 20, 55, 57, 80, 82, and 85 are relative terms which render the claims indefinite. The term is not defined by the claims, the Specification does not provide a reasonable standard for ascertaining the requisite degree, and thus one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Since no guidance is provided as to how much "above" a given value is and still falls within the scope of the instantly claimed subject matter as

circumscribed by the term "near", the metes and bounds of the terms are not clear, making it impossible to ascertain with reasonable precision when the terms are infringed and when they are not.

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 1, 3, 5, 7, 12, 13, 16-36, 38, 40, 42, 47, 48, 51-65, 67, 69, 71, 76-88, 90, 92 and 97-99 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

Claims 1 and 65 recite "line emission x-rays of an energy selected to cause emission of Auger electrons from said pre-selected element [Pt] of said compound [cisplatin] in a dose effective to disrupt DNA proximate to the irradiated pre-selected element". Claims 20, 22, 55, 57, 80, 82, and 85 recite "wherein the target and the e-beam energy are selected to provide substantially monochromatic line emission x-rays having an energy above and near the K-absorption edge" (Claims 20, 55, 80, and 85), or "L-absorption edge" (Claim 22, 57, 82, and 85) "of the pre-selected element [Pt] of the compound [cisplatin]" (emphasis added). The Specification does not disclose the energy of line emission x-rays required to cause emission of Auger electrons from the platinum in the elected compound, cisplatin. The Specification does not disclose the K-

absorption edge or L-absorption edge for platinum. Additionally, the Specification does not disclose a target and e-beam energy combination necessary to provide substantially monochromatic line emission x-rays having an energy above and near the K-absorption or L-absorption edge of platinum. Therefore, the disclosed claims are rejected for failing to meet the written description requirement.

Claim 98 recites a "method according to claim 85, wherein the pre-selected element of the compound has an atomic number in the range of from 35 to 83. The Specification discloses an atomic number range of 35 to 79, not a range of 35-83.

Claims 30-35 recite a method of treating malfunctioning cells which have been removed from a mammal and then returned to the mammal after said treatment. The Specification does not disclose any steps necessary to practice this method aside from a disclosure of the possibility of its use. There is no evidence that at the time of the invention the Applicant had possession of this part of the claimed invention.

11. Claims 1, 3, 5, 7, 12, 13, 16-36, 38, 40, 42, 47, 48, 51-65, 67, 69, 71, 76-88, 90, 92 and 97-99 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

> The factors to be considered in determining whether a disclosure meets the enablement requirements of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir., 1988). The court in Wands states, "Enablement is not precluded by the necessity for some experimentation, such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue', not 'experimentation'" (*Wands*, 8 USPQ2sd 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required

to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations" (*Wands*, 8 USPQ2d 1404). Among these factors are: (1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

While all of these factors are considered, a sufficient amount for a *prima facie* case is discussed below.

The instant specification fails to provide guidance that would allow the skilled artisan to practice that instant invention without resorting to undue experimentation in view of further discussion below.

The nature of the invention and the breadth of the claims:

The claimed invention relates to a method of treating malfunctioning cells, including tumors or cancer, in a living mammal, with comprises the steps of: (a) administering a compound (e.g., cisplatin) which associates with DNA in cells of said mammal, wherein said compound comprises a pre-selected element (e.g., platinum); and then (b) irradiating the select region in which malfunctioning cells, having said compound associated with DNA, are located, with line emission x-rays of an energy selected to cause emission of Auger electrons from said pre-selected element of said compound in a dose effective to cause ~~disrupt~~ disruption of DNA proximate to the irradiated pre-selected element.

The claims are very broad and inclusive to all types of tumors, cancers, polyps, pre-cancerous cells, and other malfunctioning cells.

The state of the prior art, relative skill of those in the art and the predictability of the art:

In just considering therapeutic treatments for cancers and tumors, the prior art teaches there is no one specific treatment that is effective for all types of cancer. See Goldman et al., Ed., Cecil Textbook of Medicine, 21st Edition, Volume 1, 2000, Table 198-5, page 1065, Table 198-6, page 1066, Table 198-8, page 1068, and Table 198-9, page 1071. One of skill in the art would also expect that different cell types would have different affinities for the selected compound of the present invention, leading to variable responsiveness to the instant methods.

The relative skill of those in the art is that of a Ph.D. or M.D.

The present invention is unpredictable given the breadth of the claims.

The amount of direction or guidance provided and the presence or absence of working examples:

Applicant's specification does not contain any working examples showing what types of malfunctioning cells were treated by the instant invention.

The quantity of experimentation necessary:

Applicant has failed to provide guidance as to how the instant invention (including specific compounds and specific chemical elements used for the e-beam target) will treat all types of abnormal cells. Therefore, undue experimentation would be required to practice the invention as it is claimed in its current scope.

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

13. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

14. Claims 1, 3, 5, 7, 12, 13, 16-36, 38, 40, 42, 47, 48, 51-65, 67, 69, 71, 76-88, 90, 92 and 97-99 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mills (U.S. Patent No. 6,224,848), in view of Wang (U.S. Patent No. 5,627,871).

Mills teaches *inter alia* a method for eliciting tissue necrosis, in treating *inter alia* cancer, by administering a compound (e.g., cisplatin) that binds to targeted tissue DNA, wherein said compound comprises an atom (e.g., platinum) that is excitable with radiation in a distinct narrow frequency band and energy level, causing an Auger electron cascade resulting in radiolysis of DNA. See Abstract and columns 108-110, claims 1, 5, and 9. Note that the compound, cis-diamminedichloroplatinum (II), taught by Mills in column 109, line 8, is the chemical name of cisplatin. Since cisplatin taught in the reference is the same as cisplatin recited by the instant invention, the properties

of the elected compound (cisplatin) recited by the instant claims would also be encompassed by the cisplatin taught by Mills. For instance, the rate of physiological excretion of cisplatin and stability against dissociation of platinum from cisplatin during the time prior to complete excretion of cisplatin (e.g., instant Claims 16 and 17 respectively) would be identical in both the reference and the instant invention. Similarly, the K- and L-absorption edge of platinum and the amount of Auger electrons released from the platinum in cisplatin would be identical in the Mills reference and the instant claims.

The instant invention differs from the cited reference in that the cited reference does not teach the Applicant's preferred method of eliciting Auger electron cascade (i.e., line emission x-rays) from the selected element (i.e., platinum). However, the secondary reference, Wang, teaches the preferred line emission x-rays to be well known in the art. See column 10, lines 27-51. Wang teaches an end window transmission x-ray tube possessing a metal foil target on said end window, the thickness and composition of the metal foil target and the e-beam energy focused thereupon generate a micro-focused bright line beam x-rays of pre-selected energy. See Abstract.

Therefore, one skilled the art would have understood that the substitution of one monochromatic x-ray source (with distinct and specific frequency and energy level properties) for another source (with the same energy properties) would produce and achieve the same results (causing a Auger electron cascade from the platinum in the cisplatin) in the absence of evidence to the contrary. It would have been obvious to the

artisan to use the x-ray source taught by Wang because of the increased convenience and logistics of using the smaller and more easily transported x-ray tube as opposed to the synchrotron taught by Mills.

The references do not teach the treatment of cells removed from and returned/transplanted back to a mammal. The references do not teach a kit comprising an x-ray tube having a target comprising a selected metal, and a compound (cisplatin) comprising a selected element (Pt).

On skilled in the art would have well versed in the practice of removing bone marrow and various other cells from the body for treating certain cancers (e.g., x-ray treatment) and returning/transplanting these cell back into the body. It would have been obvious to use the methods taught by Mills and modified by the teachings of Wang to seek an improved cancer therapy. It would also have been obvious to said artisan to "package" the essential components necessary to practice these methods. One would have been motivated to do so to provide a more convenient and efficient means for practicing a method of cancer therapeutics.

Conclusion

15. Claims 1, 3, 5, 7, 12, 13, 16-36, 38, 40, 42, 47, 48, 51-65, 67, 69, 71, 76-88, 90, 92 and 97-99 are rejected.

16. No claims are allowed.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gregg Polansky whose telephone number is (571) 272-9070. The examiner can normally be reached on Mon-Thur 8:30 A.M. - 7:00 P.M. EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Gregg Polansky

Phyllis Spivack 11/22/07

PHYLLIS SPIVACK
PRIMARY EXAMINER